

Amendments to the Specification

Please delete all of the paragraphs starting at page 29, line 14 through page 31, line 3, which were previously amended in the response and amendment deposited on September 8, 2003, and replace those paragraphs with the following:

Brief Description of the Drawings

Some embodiments of the invention will now be described with reference to the accompanying drawings in which:

Fig 1 is a diagram showing the functioning of 6-deoxyerythronolide B synthase (DEBS), a modular PKS producing 6-deoxyerythronolide B (6-DEB) a precursor of erythromycin A.

Figs. 2A-2D give the amino acid sequence comparison of the KS domains and the CLF domains of representative Type II PKS gene clusters. The active site Cysteine (C) of the KS domains is arrowed in the Figure and aligns with the Glutamine (Q) or glutamic acid (E) of the CLF domains. The abbreviations used, and the relevant Genbank/EMBL accession numbers are: GRA: granaticin from *Streptomyces violaceoruber* (X63449); HIR: unknown polyketide from *Saccharopolyspora hirsuta* (M98258); ACT, actinorhodin from *Streptomyces coelicolor* (X63449); CIN: unknown polyketide from *Streptomyces cinnamonensis* (Z11511); VNZ: jadomycin from *Streptomyces venezuelae* (L33245); NOG: anthracyclines from *Streptomyces nogalater* (Z48262); TCM: tetracenomycin from *S. glaucescens* (M80674); DAU: daunomycin from *Streptomyces* sp. C5 (L34880); PEU, doxorubicin from *Streptomyces peucetius* (L35560); WHI: WhiE spore pigment from *Streptomyces coelicolor* (X55942). From top to bottom, the sequences are SEQ ID NOs: 1-20, respectively.

Fig 3A shows the gene organization of the PKSs for ~~three the~~ 16-membered ring macrolides[[,]] tylosin[[,]] and spiramycin and niddamycin. Fig 3B shows the gene organization

of the PKS for the 16-membered ring macrolide niddamycin.

Figs. 4A-4C show the amino acid sequence alignment of KSq-ATq loading didomains of the PKSs for niddamycin (SEQ ID NO: 21), platenolide(spiramycin) (SEQ ID NO: 22), monensin (SEQ ID NO: 23), oleandomycin (SEQ ID NO: 24) and tylosin (SEQ ID NO: 25). The sequences for the monensin and oleandomycin loading didomains have not been previously disclosed. The arrow in Figure 4B indicates the conserved arginine residue.

Fig. 5 The enzymatic steps that convert 6-deoxyerythronolide B into erythromycin A in *Saccharopolyspora erythraea*.

Fig. 6 is a diagram showing the construction of plasmid pJLK117.

Fig. 7 shows the structures of two oligonucleotides. The forward and backward oligonucleotides are SEQ ID NOs: 26 and 27, respectively, and are shown as annealed with restriction enzyme sites.